Complete Summary

GUIDELINE TITLE

The perioperative management of antithrombotic therapy. American College of Chest Physicians evidence-based clinical practice guidelines (8th edition).

BIBLIOGRAPHIC SOURCE(S)

Douketis JD, Berger PB, Dunn AS, Jaffer AK, Spyropoulos AC, Becker RC, Ansell J. The perioperative management of antithrombotic therapy: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008 Jun;133(6 Suppl):299S-339S. [237 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- December 3, 2008, Innohep (tinzaparin): The U.S. Food and Drug Administration (FDA) has requested that the labeling for Innohep be revised to better describe overall study results which suggest that, when compared to unfractionated heparin, Innohep increases the risk of death for elderly patients (i.e., 70 years of age and older) with renal insufficiency. Healthcare professionals should consider the use of alternative treatments to Innohep when treating elderly patients over 70 years of age with renal insufficiency and deep vein thrombosis (DVT), pulmonary embolism (PE), or both.
- February 28, 2008, Heparin Sodium Injection: The U.S. Food and Drug Administration (FDA) informed the public that Baxter Healthcare Corporation has voluntarily recalled all of their multi-dose and single-use vials of heparin sodium for injection and their heparin lock flush solutions. Alternate heparin manufacturers are expected to be able to increase heparin production sufficiently to supply the U.S. market. There have been reports of serious adverse events including allergic or hypersensitivity-type reactions, with symptoms of oral swelling, nausea, vomiting, sweating, shortness of breath, and cases of severe hypotension.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Arterial and venous thromboembolism

GUIDELINE CATEGORY

Management
Prevention
Treatment

CLINICAL SPECIALTY

Anesthesiology
Cardiology
Critical Care
Emergency Medicine
Family Practice
Hematology
Internal Medicine
Neurology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Nurses
Patients
Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Social Workers

GUIDELINE OBJECTIVE(S)

- To provide recommendations for the perioperative management of patients who are receiving vitamin K antagonists (VKAs) or antiplatelet drugs, such as aspirin and clopidogrel, and require an elective surgical or other invasive procedures
- To provide recommendations for the perioperative use of bridging anticoagulation, typically with low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH)
- A secondary objective is to address the perioperative management of such patients who require urgent surgery

TARGET POPULATION

Patients requiring perioperative antithrombotic therapy for the treatment and prevention of arterial and venous thromboembolism

INTERVENTIONS AND PRACTICES CONSIDERED

1. Perioperative interruption of vitamin K antagonists (VKAs) prior to surgery
2. Post-operative resumption of VKAs
3. Oral vitamin K (in patients whose international normalized ratio [INR] is still elevated following interruption of VKAs)
4. Bridging anticoagulation (subcutaneous low molecular weight heparin [SC LMWH], intravenous unfractionated heparin [IV UFH])
5. Perioperative interruption of antiplatelet therapy (aspirin, clopidogrel)
    - Patients with coronary stents
    - Patients undergoing dental, dermatological, ophthalmological procedures
    - Patients undergoing urgent surgical procedures (oral vitamin K, fresh frozen plasma, platelet transfusion)
6. Post-operative resumption of antiplatelet therapy

MAJOR OUTCOMES CONSIDERED

- Mortality
- Incidence of thrombosis
- Recurrent thromboembolism
- Incidence of major and minor hemorrhage
- Time to achieve therapeutic international normalized ratio (INR)
- Anticoagulant response

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Process of Searching for Evidence

Defining the clinical question provided the framework for formulating eligibility criteria that guided the search for relevant evidence. In specifying eligibility criteria, authors identified not only patients, interventions, and outcomes, but also methodologic criteria. For many recommendations, authors restricted eligibility to randomized controlled trials (RCTs).

For many questions, randomized trials did not provide sufficient data, and chapter authors included observational studies when randomized trials were not the most appropriate design to address the research question. In particular, randomized trials are not necessarily the best design to understand risk groups, that is, the baseline or expected risk of a given event for certain subpopulations. Because no interventions are typically examined in questions about prognosis, one replaces interventions by the duration of exposure measured in time.

Identifying the Evidence

To identify the relevant evidence, a team of librarians and research associates at the McMaster University Evidence based practice center (EPC) conducted comprehensive literature searches. Methodologic experts (including the editors) and the EPC librarians reviewed each question to ensure the development of a comprehensive search strategy. For example, for questions about antiplatelet agents, the EPC consulted chapter authors to ensure that the search included all relevant antiplatelet agents. More specifically, authors then decided whether to include dipyridamole in a search that already included aspirin, clopidogrel, and ticlopidine.

For each question the authors provided, the librarians searched the Cochrane Database of Systematic Reviews, MEDLINE, and Embase for published English-language literature and human studies between 2002 and May 2006. To filter MEDLINE and Embase search results for RCT evidence, the librarians used the search strategy developed by the Cochrane Collaboration. These searches updated the more comprehensive and sensitive searches conducted for the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy: Evidence Based Guidelines.

The EPC team conducted separate searches for systematic reviews; RCTs; and, if applicable, observational studies. For observational studies, searches were not restricted in terms of methodology. Although increasing the probability of identifying all published studies, this sensitive approach resulted in large numbers of citations for many of the defined clinical questions. Therefore, trained research assistants screened the citation list developed from the search using criteria of increased specificity to reduce the number of irrelevant citations that the authors received. These irrelevant citations included press news, editorials, narrative reviews, single-case reports, studies that included fewer participants than specified by authors as an inclusion criterion, animal studies (any nonhuman studies), and letters to the editor. Authors did not include data from abstracts of meetings for the development of recommendations, and the guideline developers did not explicitly use Internet sources to search for research data. Authors were encouraged, however, to mention abstracts that reported on groundbreaking data that were particularly relevant to a specific question in the chapters in order to alert readers that new, fully published evidence might become available shortly.

Standard Consideration of Study Quality

High-quality clinical guidelines should pay careful attention to the methodologic quality of the studies that form the basis of their recommendations. Using the example of the prevention of venous thromboembolism during air travel, Table 1 in the methodology companion (see "Availability of Companion Documents" field) shows the criteria for assessment of study quality (randomization, concealment or treatment allocation, blinding, completeness of follow-up, and whether the analysis was performed according to the intention-to-treat principle), and Table 2 in the methodology companion (see "Availability of Companion Documents" field) shows the presentation of results that were circulated to the authors. Whereas all authors attended to these criteria, the guideline developers have summarized the results of the quality assessment for only a minority of the recommendations. Readers can find these summaries in an online appendix to the recommendations (see online supplemental data).

In assessing the quality of observational studies, the guideline developers did not make a distinction between prospective and retrospective because the key issues are unbiased sampling, high-quality measurement of patient characteristics and outcomes, and complete follow-up.

Although it is more likely that these quality criteria will be achieved in prospective studies, prospective studies may fail to achieve them, and retrospective studies may succeed. The guideline developers did make a key distinction about whether internal comparisons exist and their nature. Studies without internal comparisons received the label "case series" unless they met the following criteria: (1) a protocol existed before the date of commencement of data collection; (2) a definition of inclusion and exclusion criteria was available; (3) the study reported the number of excluded patients; (4) the study conducted a standardized follow-up, including description of schedule of follow-up, investigation of suspected outcomes, and criteria used to define outcomes; and (5) the study reported all losses to follow-up.

The guideline developers labeled studies that met these criteria "cohort studies without internal controls." Studies with internal comparisons received the label "cohort studies with concurrent controls" or "cohort studies with historical controls." These cohort studies may succeed or fail to ensure settings, similar time frames, adjustment for differences in patients' characteristics, and follow-up with patients. These features were captured in descriptive tables provided to authors when requested from the EPC.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The rating scheme framework captures the trade-off between benefits and risks (1 or 2) and the methodological quality of the underlying evidence (A, B, or C). See "Grades of recommendations for antithrombotic agents" in the "Availability of Companion Documents" field and the "Rating Scheme for the Strength of the Recommendations." field.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Summarizing Evidence

The electronic searches also included searches for systematic reviews. If authors were satisfied with a recent high-quality systematic review, evidence from that review provided a foundation for the relevant recommendation.

Pooled analyses from high-quality systematic reviews formed summary data on which panelists based their recommendations wherever possible. Pooling offers the advantage of obtaining more precise estimates of treatment effects and allows for greater generalizability of results. However, pooling also bears the risk of spurious generalization. In general, the summary estimates of interest were the different types of outcomes conveying benefits and downsides (risk, burden, and cost). When pooled estimates of effects were not available, the McMaster University Evidence based practice center (EPC) conducted meta-analysis to obtain pooled estimates for specific questions. These were questions that authors had specifically identified.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Group-Specific Recommendations

In general, the guideline developers have endeavored to make their recommendations as specific as possible for patient subgroups differing according to risk. Whenever valid prognostic data were available, the guideline developers used them to estimate absolute effects and made recommendations accordingly. Unfortunately, reliable prognostic indexes are not usually available, limiting the extent to which such group-specific recommendations are possible.

Acknowledge Values and Preferences and Resource Use Underlying Recommendations

Under ideal circumstances, knowledge of average patient values and preferences would be available for every recommendation, the panel members would

summarize these values and preferences, and they would be integrated into the recommendations that guideline developers make. The guideline developers asked all chapter chairs before beginning the searches for the relevant literature to identify recommendations that they believed were particularly sensitive to patients' values and preferences. Moderate-quality evidence regarding values and preferences bearing directly on the recommendations proved available for only the chapter that addresses antithrombotic therapy in patients with atrial fibrillation. The panelists bore in mind what average patient values and preferences may be; the process, however, is speculative.

The guideline developer's main strategy for dealing with this unsatisfactory situation is to make the values and preferences underlying the recommendations explicit whenever the panelists believed that value and preference issues were crucial for a recommendation.

In addition, the guideline developers involved three consultants with expertise in the area of values and preferences to collaborate with the chairs of two chapters and try to ensure that the guidelines adequately represented the views of patients. This collaboration led to extensive discussions among the chapter authors and the consultants and the reflection of these discussions in the associated values and preference statements.

Finalizing and Harmonizing Recommendations

After having completed the steps the guideline developers have described above, the guideline authors formulated draft recommendations before the conference, which laid the foundation for authors to work together and critique the recommendations. Figure 1 in the methodology companion (see "Availability of Companion Documents" field) shows the process of guideline development and review. Drafts of chapters that included draft recommendations were usually distributed for peer review to at least two panel members and were always reviewed by at least one panel editor before the conference. Written critiques were prepared and returned to the authors for revision of their work. At the plenary conference, a representative of each chapter presented potentially controversial issues in their recommendations. Chapter authors met to integrate feedback and consider related recommendations in other chapters and to revise their own guidelines accordingly. Authors continued this process after the conference until they reached agreement within their groups and with other author groups who provided critical feedback. The editors of this supplement harmonized the chapters and resolved remaining disagreements between chapters through facilitated discussion. All major correspondence and discussions at the meeting were recorded in written and audio protocols and are publicly available.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grading Recommendation

Grade of Recommendation*	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
Strong recommendation, high-quality evidence, Grade 1A	Desirable effects clearly outweigh undesirable effects, or *vice versa*	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; further research is very unlikely to change our confidence in the estimate of effect
Strong recommendation, moderate-quality evidence, Grade 1B	Desirable effects clearly outweigh undesirable effects, or *vice versa*	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; higher quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate
Strong recommendation, low or very low-quality evidence, Grade 1C	Desirable effects clearly outweigh undesirable effects, or *vice versa*	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate
Weak recommendation, high-quality evidence, Grade 2A	Desirable effects closely balanced with undesirable effects	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	The best action may differ depending on circumstances or patient or society values; further research is very unlikely to change our confidence in the estimate of effect
Weak recommendation, moderate-quality evidence, Grade 2B	Desirable effects closely balanced with undesirable effects	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very	Best action may differ depending on circumstances or patient or society values; higher-quality research may well have an important impact on our confidence in the

Grading Recommendation			
Grade of Recommendation*	**Benefit vs. Risk and Burdens**	**Methodologic Quality of Supporting Evidence**	**Implications**
		strong evidence from observational studies	estimate of effect and may change the estimate
Weak recommendation, low or very low-quality evidence, Grade 2C	Desirable effects closely balanced with undesirable effects	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Other alternatives may be equally reasonable; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate

*The guideline developers use the wording *recommend* for strong (Grade 1) recommendations and *suggest* for weak (Grade 2) recommendations.

COST ANALYSIS

For these guidelines, the guideline developers implemented recommendations of a recent American College of Chest Physicians (ACCP) task force on integrating resource allocation in clinical practice guidelines by restricting resource expenditure consideration to a small number of recommendations for which they were particularly relevant. The guideline developers relied on two consultants with expertise in economic assessment to help with the process of considering costs in those small numbers of recommendations that the guideline developers considered very important to the decision.

Recommendations highly sensitive to resource allocation now include value and preference statements regarding how cost issues were integrated.

Refer to "Strategies for incorporating resource allocation and economic considerations" (see "Availability of Companion Documents" field) for details of the cost analyses.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The American College of Chest Physicians (ACCP) Health Science Policy (HSP) established a process for the thorough review of all ACCP evidence-based clinical practice guidelines. After final review by the editors, the guidelines underwent

review by appropriate NetWorks of the ACCP (for these guidelines, the Cardiovascular and Pulmonary Vascular NetWorks), the HSP, and the Board of Regents. The latter two have the right of approval or disapproval but usually work with the guideline authors and editors to make necessary revisions before final approval. Each group identified primary reviewers who read the full set of chapters as well as individual committee members who were responsible for reviewing one or more chapters. The reviewers considered both content and methodology as well as whether there was balanced, not biased, reporting and adherence to HSP processes. Finally, the *CHEST* editor-in-chief read and forwarded the manuscripts for nonbiased, independent, external peer review before acceptance for publication.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The grades of recommendation (1A, 1B, 1C, 2A, 2B, 2C) are defined at the end of the "Major Recommendations" field.

Perioperative Management of Patients Who Are Receiving Vitamin K Antagonists (VKAs)

1. In patients who require temporary interruption of a VKA before surgery or a procedure and require normalization of the international normalized ratio (INR) for the surgery or procedure, the guideline developers recommend stopping VKAs approximately 5 days before surgery over stopping VKAs within a shorter time interval before surgery to allow adequate time for the INR to normalize **(Grade 1B)**.
2. In patients who have had temporary interruption of a VKA before surgery or a procedure, the guideline developers recommend resuming VKAs approximately 12 to 24 hours (the evening of or the next morning) after surgery and when there is adequate hemostasis over resumption of VKAs closer to surgery **(Grade 1C)**.
3. In patients who require temporary interruption of a VKA before surgery or a procedure and whose INR is still elevated (i.e., $\geq$1.5) 1 to 2 days before surgery, the guideline developers suggest administering low-dose (i.e., 1 to 2 mg) oral vitamin K to normalize the INR instead of not administering vitamin K **(Grade 2C)**.
4. In patients with a mechanical heart valve or atrial fibrillation or venous thromboembolism (VTE) at high risk for thromboembolism, the guideline developers recommend bridging anticoagulation with therapeutic-dose subcutaneous (SC) low-molecular-weight heparin (LMWH) or intravenous (IV) unfractionated heparin (UFH) over no bridging during temporary interruption of VKA therapy **(Grade 1C)**; the guideline developers suggest therapeutic-dose SC LMWH over IV UFH **(Grade 2C)**. In patients with a mechanical heart valve or atrial fibrillation or VTE at moderate risk for thromboembolism, the guideline developers suggest bridging anticoagulation with therapeutic-dose SC LMWH, therapeutic-dose IV UFH, or low-dose SC LMWH over no bridging during temporary interruption of VKA therapy **(Grade 2C)**; the guideline developers suggest therapeutic-dose SC LMWH over other management options **(Grade 2C)**. In patients with a mechanical heart valve or atrial fibrillation or VTE at low risk for thromboembolism, the guideline developers

suggest low-dose SC LMWH or no bridging over bridging with therapeutic-dose SC LMWH or IV UFH **(Grade 2C)**.

Underlying values and preferences: In patients at high or moderate risk for thromboembolism, the recommendations reflect a relatively high value on preventing thromboembolism and a relatively low value is on preventing bleeding; in patients at low risk for thromboembolism, the recommendations reflect a relatively high value on preventing bleeding and a relatively low value on preventing thromboembolism.

Perioperative Management of Patients Who Are Receiving Bridging Anticoagulation

1. In patients who require temporary interruption of VKAs and are to receive bridging anticoagulation, from a cost-containment perspective the guideline developers recommend the use of subcutaneous (SC) low-molecular-weight heparin (LMWH) administered in an outpatient setting where feasible instead of inpatient administration of intravenous (IV) unfractionated heparin (UFH) **(Grade 1C)**.

   Underlying values and preferences: This recommendation reflects a consideration not only of the trade-off between the advantages and disadvantages of SC LMWH and IV UFH as reflected in their effects on clinical outcomes (LMWH at least as good, possibly better), but also the implications in terms of resource use (costs) in a representative group of countries (substantially less resource use with LMWH).

2. In patients who are receiving bridging anticoagulation with therapeutic-dose SC LMWH, the guideline developers recommend administering the last dose of LMWH 24 hours before surgery or a procedure over administering LMWH closer to surgery **(Grade 1C)**; for the last preoperative dose of LMWH, the guideline developers recommend administering approximately half the total daily dose instead of 100% of the total daily dose **(Grade 1C)**. In patients who are receiving bridging anticoagulation with therapeutic-dose IV UFH, the guideline developers recommend stopping UFH approximately 4 hours before surgery over stopping UFH closer to surgery **(Grade 1C)**
3. In patients undergoing a minor surgical or other invasive procedure and who are receiving bridging anticoagulation with therapeutic-dose LMWH, the guideline developers recommend resuming this regimen approximately 24 hours after (e.g., the day after) the procedure when there is adequate hemostasis over a shorter (e.g., < 12 hours) time interval **(Grade 1C)**. In patients undergoing major surgery or a high bleeding risk surgery/procedure and for whom postoperative therapeutic-dose LMWH/UFH is planned, the guideline developers recommend either delaying the initiation of therapeutic-dose LMWH/UFH for 48 to 72 hours after surgery when hemostasis is secured, administering low-dose LMWH/UFH after surgery when hemostasis is secured, or completely avoiding LMWH or UFH after surgery over the administration of therapeutic-dose LMWH/UFH in close proximity to surgery **(Grade 1C)**. The guideline developers recommend considering the anticipated bleeding risk and adequacy of postoperative hemostasis in individual patients to determine the timing of LMWH or UFH resumption after surgery instead of resuming LMWH or UFH at a fixed time after surgery in all patients **(Grade 1C)**.

4. In patients who are receiving bridging anticoagulation with LMWH, the guideline developers suggest against the routine use of anti-factor Xa levels to monitor the anticoagulant effect of LMWHs **(Grade 2C)**.

Perioperative Management of Patients Who Are Receiving Antiplatelet Therapy

1. In patients who require temporary interruption of aspirin-or clopidogrel-containing drugs before surgery or a procedure, the guideline developers suggest stopping this treatment 7 to 10 days before the procedure over stopping this treatment closer to surgery **(Grade 2C)**.
2. In patients who have had temporary interruption of aspirin therapy because of surgery or a procedure, the guideline developers suggest resuming aspirin approximately 24 hours (or the next morning) after surgery when there is adequate hemostasis instead of resuming aspirin closer to surgery **(Grade 2C)**. In patients who have had temporary interruption of clopidogrel because of surgery or a procedure, we suggest resuming clopidogrel approximately 24 hours (or the next morning) after surgery when there is adequate hemostasis instead of resuming clopidogrel closer to surgery **(Grade 2C)**.
3. In patients who are receiving antiplatelet drugs, the guideline developers suggest against the routine use of platelet function assays to monitor the antithrombotic effect of aspirin or clopidogrel **(Grade 2C)**.
4. For patients who are not at high risk for cardiac events, the guideline developers recommend interruption of antiplatelet drugs **(Grade 1C)**. For patients at high risk of cardiac events (exclusive of coronary stents) scheduled for noncardiac surgery, the guideline developers suggest continuing aspirin up to and beyond the time of surgery **(Grade 2C)**; if patients are receiving clopidogrel, the guideline developers suggest interrupting clopidogrel at least 5 days and, preferably, within 10 days prior to surgery **(Grade 2C)**. In patients scheduled for coronary artery bypass grafting (CABG), the guideline developers recommend continuing aspirin up to and beyond the time of CABG **(Grade 1C)**; if aspirin is interrupted, the guideline developers recommend it be reinitiated between 6 hours and 48 hours after CABG **(Grade 1C)**. In patients scheduled for CABG, the guideline developers recommend interrupting clopidogrel at least 5 days and, preferably, 10 days prior to surgery **(Grade 1C)**. In patients scheduled for percutaneous coronary intervention (PCI), the guideline developers suggest continuing aspirin up to and beyond the time of the procedure; if clopidogrel is interrupted prior to PCI, the guideline developers suggest resuming clopidogrel after PCI with a loading dose of 300 to 600 mg **(Grade 2C)**.
5. In patients with a bare metal coronary stent who require surgery within 6 weeks of stent placement, the guideline developers recommend continuing aspirin and clopidogrel in the perioperative period **(Grade 1C)**. In patients with a drug-eluting coronary stent who require surgery within 12 months of stent placement, the guideline developers recommend continuing aspirin and clopidogrel in the perioperative period **(Grade 1C)**. In patients with a coronary stent who have interruption of antiplatelet therapy before surgery, the guideline developers suggest against the routine use of bridging therapy with UFH, LMWH, direct thrombin inhibitors, or glycoprotein IIb/IIIa inhibitors **(Grade 2C)**.

Underlying values and preferences: These recommendations reflect a relatively high value placed on preventing stent-related coronary thrombosis, a consideration of complexity and costs of administering bridging therapy in the absence of efficacy and safety data in this clinical setting, and a relatively low value on avoiding the unknown but potentially large increase in bleeding risk associated with the concomitant administration of aspirin and clopidogrel during surgery.

Perioperative Management of Antithrombotic Therapy in Patients Who Require Dental, Dermatologic, or Ophthalmologic Procedures

1. In patients who are undergoing minor dental procedures and are receiving VKAs, the guideline developers recommend continuing VKAs around the time of the procedure and coadministering an oral prohemostatic agent **(Grade 1B)**. In patients who are undergoing minor dental procedures and are receiving aspirin, the guideline developers recommend continuing aspirin around the time of the procedure **(Grade 1C)**. In patients who are undergoing minor dental procedures and are receiving clopidogrel, please refer to the recommendations outlined in (See recommendations 5 and 6 in the "Perioperative Management of Patients Who Are Receiving Antiplatelet Therapy" section above.)
2. In patients who are undergoing minor dermatologic procedures and are receiving VKAs, the guideline developers recommend continuing VKAs around the time of the procedure **(Grade 1C)**. In patients who are undergoing minor dermatologic procedures and are receiving aspirin, the guideline developers recommend continuing aspirin around the time of the procedure **(Grade 1C)**. In patients who are undergoing minor dermatologic procedures and are receiving clopidogrel, (please refer to recommendations 5 and 6 in the "Perioperative Management of Patients Who Are Receiving Antiplatelet Therapy" section above.)
3. In patients who are undergoing cataract removal and are receiving VKAs, the guideline developers recommend continuing VKAs around the time of the procedure **(Grade 1C)**. In patients who are undergoing cataract removal and are receiving aspirin, the guideline developers recommend continuing aspirin around the time of the procedure **(Grade 1C)**. In patients who are undergoing cataract removal and are receiving clopidogrel, please refer to recommendations 5 and 6 in the "Perioperative Management of Patients Who Are Receiving Antiplatelet Therapy" section above.)

Perioperative Management of Antithrombotic Therapy Patients Who Require Urgent Surgical or Other Invasive Procedures

1. In patients who are receiving VKAs and require reversal of the anticoagulant effect for an urgent surgical or other invasive procedure, the guideline developers recommend treatment with low-dose (2.5 to 5.0 mg) IV or oral vitamin K **(Grade 1C)**. For more immediate reversal of the anticoagulant effect, the guideline developers suggest treatment with fresh-frozen plasma or another prothrombin concentrate in addition to low-dose IV or oral vitamin K **(Grade 2C)**.
2. For patients receiving aspirin, clopidogrel, or both, are undergoing surgery and have excessive or life-threatening perioperative bleeding, the guideline

developers suggest transfusion of platelets or administration of other prohemostatic agents **(Grade 2C)**.

Definitions:

Grading Recommendation			
Grade of Recommendation*	**Benefit vs. Risk and Burdens**	**Methodologic Quality of Supporting Evidence**	**Implications**
Strong recommendation, high-quality evidence, Grade 1A	Desirable effects clearly outweigh undesirable effects, or *vice versa*	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; further research is very unlikely to change our confidence in the estimate of effect
Strong recommendation, moderate-quality evidence, Grade 1B	Desirable effects clearly outweigh undesirable effects, or *vice versa*	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; higher quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate
Strong recommendation, low or very low-quality evidence, Grade 1C	Desirable effects clearly outweigh undesirable effects, or *vice versa*	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate
Weak recommendation, high-quality evidence, Grade 2A	Desirable effects closely balanced with undesirable effects	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	The best action may differ depending on circumstances or patient or society values; further research is very unlikely to change our confidence in the estimate of effect
Weak	Desirable	Evidence from RCTs	Best action may differ

Grading Recommendation			
Grade of Recommendation*	**Benefit vs. Risk and Burdens**	**Methodologic Quality of Supporting Evidence**	**Implications**
recommendation, moderate-quality evidence, Grade 2B	effects closely balanced with undesirable effects	with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	depending on circumstances or patient or society values; higher-quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate
Weak recommendation, low or very low-quality evidence, Grade 2C	Desirable effects closely balanced with undesirable effects	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Other alternatives may be equally reasonable; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate

*The guideline developers use the wording *recommend* for strong (Grade 1) recommendations and *suggest* for weak (Grade 2) recommendations.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate monitoring and management of patients who require perioperative treatment with antithrombotic therapy

POTENTIAL HARMS

Antithrombotic therapy is associated with minor and major hemorrhagic events.

CONTRAINDICATIONS

CONTRAINDICATIONS

Low molecular weight heparin is contraindicated in patients with severe renal insufficiency.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Limitations of These Guideline Development Methods

Limitations of these guidelines include the limited quantity and quality of available studies for some patient groups. Second, it is possible that some authors followed this methodology more closely than others, although the development process was centralized by an evidence-based practice center (EPC) and supervised by the editors. Third, it is possible that the guideline developers missed relevant studies in spite of the comprehensive searching process. Fourth, despite their efforts to begin centralizing the methodologic evaluation of all studies to facilitate uniformity in the validity assessments of the research incorporated into these guidelines, resources were insufficient to conduct this evaluation for all but a few of the recommendations in each chapter. Fifth, the guideline developers performed only few statistical pooling exercises of primary study results. Finally, sparse data on patient preferences and values represent additional limitations inherent to most guideline development methods.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy includes local educational programs and tools offered through the American College of Chest Physicians (ACCP) Board of Governors and select other locations. The Veterans Administration (VA) will also participate in a pilot project.

IMPLEMENTATION TOOLS

Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Douketis JD, Berger PB, Dunn AS, Jaffer AK, Spyropoulos AC, Becker RC, Ansell J. The perioperative management of antithrombotic therapy: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008 Jun;133(6 Suppl):299S-339S. [237 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2008 Jun

GUIDELINE DEVELOPER(S)

American College of Chest Physicians - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Chest Physicians

GUIDELINE COMMITTEE

American College of Chest Physicians (ACCP) Expert Panel on Antithrombotic and Thrombolytic Therapy

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Authors: James D. Douketis, MD, FRCP(C); Peter B. Berger, MD, FACP; Andrew S. Dunn, MD, FACP; Amir K. Jaffer, MD; Alex C. Spyropoulos, MD, FACP, FCCP; Richard C. Becker, MD, FACP, FCCP; and Jack Ansell, MD, FACP, FCCP

Committee Co-Chairs: Jack Hirsh, MD, FCCP (*Chair*); Gordon H. Guyatt, MD, FCCP; Gregory W. Albers, MD; Robert A. Harrington, MD, FCCP; Holger J. Schünemann, MD, PhD, FCCP

Participants: Giancarlo Agnelli, MD; Pierre Amarenco, MD; Jack E. Ansell, MD; Collin Baigent; Shannon M. Bates, MD; Kenneth A. Bauer, MD; Richard C. Becker, MD; Peter B. Berger, MD; David Bergqvist, MD, PhD; Rebecca J. Beyth, MD; Christopher P. Cannon, MD; Elizabeth A. Chalmers, MB, ChB, MD; Anthony K.C. Chan, MBBS; Clifford W. Colwell, Jr., MD; Anthony J. Comerota, MD; Deborah Cook, MD; Mark A. Crowther, MD; James E. Dalen, MD; Gabrielle deVeber, MD, MHSc; Maria Benedetta Donati, MD, PhD; James D. Douketis, MD; Andrew Dunn, MD; J. Donald Easton, MD; Michael Ezekowitz, MD; Margaret Fang; William H. Geerts, MD, FCCP; Alan S. Go, MD; Samuel Z. Goldhaber, MD, FCCP; Shaun D. Goodman, MD; Michael Gould, MD, FCCP; Ian A. Greer, MD; Andreas Greinacher, MD; David Gutterman, MD, FCCP, HSP; Jonathan L. Halperin, MD; John A. Heit, MD; Elaine M. Hylek, MD; Alan Jacobson, MD; Roman Jaeschke, MD, PhD; Amir K. Jaffer, MD; Susan Kahn; Clive Kearon, MBBCh, PhD; Fenella Kirkham, MBBC; Andreas Koster, MD, PhD; Michael R. Lassen, MD; Mark N. Levine, MD, MSc; Sandra Zelman Lewis, PhD; A. Michael Lincoff, MD; Gregory YH Lip, MD; Christopher Madias, MD; Warren J. Manning, MD; Daniel B. Mark, MD; M. Patricia Massicotte, MD, MSc; David Matchar, MD; Thomas W. Meade, DM, FCCP; Venu Menon, MD; Tracy Minichiello, MD; Paul Monagle, MBBS, MSc, MD, FCCP; Christopher M. O'Connor, MD; Patrick O'Gara, MD; E. Magnus Ohman, MD; Ingrid Pabinger, MD; Gualtiero Palareti, MD; Carlo Patrono, MD; Stephen G. Pauker, MD; Graham F. Pineo, MD; Jeffrey J. Popma, MD; Gary Raskob, PhD; Gerald Roth, MD; Ralph L. Sacco, MD; Deeb N. Salem, MD, FCCP; Charles-Marc Samama, MD, FCCP; Meyer Michel Samama, MD; Sam Schulman, MD, PhD; Daniel Singer, MD; Michael Sobel, MD; Shoshanna Sofaer, DrPH; Alex C. Spyropoulos, MD FCCP; Ph. Gabriel Steg, MD; Philip Teal, MD; Raymond Verhaeghe, MD; David A. Vorchheimer, MD; Theodore E. Warkentin, MD; Jeffrey Weitz, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Dr. Ansell discloses that he has received consultant fees from Bristol-Myers Squibb, Roche Diagnostics, and International Technidyne Corporation. He is also on the speakers bureau for Roche Diagnostic Corporation and Sanofi-Aventis, and is the past president of the Anticoagulation Forum.

Dr. Douketis reveals no real or potential conflicts of interest or commitment.

Dr. Dunn discloses that he received grant monies from and is on the speakers bureau for Sanofi-Aventis. He has also served on advisory committees for Sanofi-Aventis, Eisai, and Roche Diagnostics.

Dr. Jaffer discloses that he has received consultant fees from Sanofi-Aventis and AstraZeneca, and that he is on the speakers bureau for Sanofi-Aventis.

Dr. Becker reveals no real or potential conflicts of interest or commitment.

Dr. Spyropoulos discloses that he has received consultant fees from Boehringer Ingelheim, and has served on the speakers bureau for Sanofi-Aventis and Eisai.

Dr. Berger discloses that he has spoken at Council on Medical Education-approved scientific symposia supported by Bristol-Myers Squibb, Sanofi-Aventis, the Medicines Company, Astra-Zeneca, Medtronic, Schering-Plough, Lilly, and Daiichi Sankyo. He has served as a consultant for PlaCor, Lilly, Daiichi Sankyo,

Molecular Insight Pharmaceuticals, and CV Therapeutics. Dr. Berger also owns equity in Lumen, Inc (a company that is developing an embolic protection device).

ENDORSER(S)

American College of Clinical Pharmacy - Medical Specialty Society
American Society of Health-System Pharmacists - Professional Association

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available to subscribers of the Chest - The Cardiopulmonary and Critical Care Journal.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

Executive Summary:

- Antithrombotic and thrombolytic therapy executive summary. Chest 2008 Jun; 133:71S-109S.

Background Articles:

- Antithrombotic and thrombolytic therapy. Chest 2008 Jun; 133:110S-112S.
- Methodology for antithrombotic and thrombolytic therapy guideline development. Chest 2008 Jun; 133:113S-122S.
- Grades of recommendation for antithrombotic agents. Chest 2008 Jun; 133:123S-131S.
- Strategies for incorporating resource allocation and economic considerations. Chest 2008 Jun; 133:132S-140S.

Electronic copies: Available to subscribers of the Chest - The Cardiopulmonary and Critical Care Journal.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

PATIENT RESOURCES

None available

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